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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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THE MCCALLUM LAW FIRM, P. C.
685 BRIGGS STREET
PO BOX 929
ERIE, CO 80516

EXAMINER	
GREENE, JAIME M	
ART UNIT	**PAPER NUMBER**
1609	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,550	WILDENBERG ET AL.	
	Examiner	Art Unit	
	Jaime M. Greene	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-34* is/are pending in the application.

4a) Of the above claim(s) *30, 31, and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-29,32 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group I in the reply filed on February 16, 2007 is acknowledged. The traversal is on the ground(s) that one of the objects of the present invention is to provide a general method of detecting aneuploidy in one or more chromosomes of a subject. In a particular embodiment, such method includes a kit that provides all of the reagents necessary to conduct such a test for aneuploidy. Therefore, since the focus of certain embodiments of the present invention is to provide a general method of detecting aneuploidy in a subject and the kit is but one way to conduct such a test, Applicant respectfully submits that this specie has unity of invention and also forms a single inventive concept. This is not found persuasive because applicant has not argued how the method and kit have unity of invention, specifically how the special technical features required for group I are also required for group II.

The requirement is still deemed proper and is therefore made FINAL.

Claims 30, 31, and 33 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on February 16, 2007.

Objections

2. The disclosure is objected to because of the following informalities: the sentence on page 23, lines 23-24 is unclear. It appears that the use of the word "microparticles" in line 23 should instead be replaced with the word "labels".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 18-29 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claim 18 is considered representative. The omitted step is the step of detecting aneuploidy, stated as the outcome of the method in the preamble of claim 18. Applicant is required to clarify. In the interest of compact prosecution, claim 18 will be treated as having the following additional step: detecting aneuploidy by comparing the signal caused by the binding of said sample and said standard to said binding agent, said aneuploidy being determined by an unequal binding.

5. Claims 32 and 34 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 32 and 34 are drawn to a method but depend from non-elected kit claim 31, and therefore the intent of the claims is unclear. Also, claims 32 and 34 are incomplete because they do not specify any active steps. Applicant is required to clarify. In the interest of compact prosecution, claim 32 will be treated as being identical to claim 20, and claim 34 will be treated as being identical to claim 22.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 18 and 26-27 rejected under 35 U.S.C. 102(b) as being anticipated by Pinkel (Pinkel, et al. US Patent Number 6,562,565). Claim 18 teaches a method of detecting aneuploidy in one or more chromosomes of a subject, comprising 1) producing a fluorescently labeled polynucleotide samples representative of the number of chromosomes in the subject; 2) producing equivalent non-aneuploid fluorescently labeled polynucleotide standards for each chromosome, said label being different from that used to label said sample; 3) mixing said sample and said standard with a limited amount of binding agent for each chromosome, wherein said binding agents comprise a polynucleotide that is complementary to said sample and said standard for each chromosome immobilized onto microparticles, and said microparticles for each chromosome are distinct on a characteristic selected from the group consisting of size and fluorescent label intensity, wherein the fluorescent label on said microparticles, if present, has a distinct emission spectrum from both the label of said sample and said standard, and wherein the presence of an aneuploidy creates a detectable signal due to non-equal binding of said sample and said standard to said binding agent; and 4) detecting aneuploidy by comparing the signal caused by the unequal binding of said sample and said standard to said binding agent. Dependent claims further require that said sample and said standard are produced from genomic DNA from a somatic cell, a reproductive cell or a gamete (claim 26), that said binding agent comprises a nucleic

acid immobilized on a microparticle, and that said nucleic acid having binding specificity for said sample and said standard (claims 27).

Pinkel teaches a method of determining copy number of target nucleic acids using target nucleic acids on a solid surface (binding agent) to which a sample comprising two sets of differentially labeled nucleic acids are hybridized and detecting the copy number (see abstract) (claim 18). Pinkel teaches that the reference probes (i.e. standard) can be genomic DNA isolated from normal cells (i.e. somatic cells) representative of the number of chromosomes in the specimen, and that comparison of the standard to test probe (i.e. sample) permits detection in variations from normal (column 3, lines 16-26) (claims 18, 26). Pinkel teaches that the nucleic acids (comprising the reference probes and test probes) are labeled with two labels that should be distinguishable (i.e. detection of aneuploidy) (column 2, lines 34-38), and that the labels are usually fluorescent labels (column 3, lines 8-9) (claim 18). Pinkel teaches hybridizing the probes to the target elements (i.e. sample and standard to binding agent) (column 11, lines 28-32), wherein the hybridization involves using immobilized target nucleic acids (column 11, lines 51-53) (claims 18, 27). Pinkel teaches that the target elements (i.e. binding agent) may be on separate supports, such as a plurality of beads (column 2, lines 55-56), and that the target elements are typically from 1μM to 3mM (i.e. microparticles, column 4, lines 26-31) (claim 18). Pinkel also teaches that beads of various sizes can be used (column 8, lines 57-61) (claim 18). Finally, Pinkel teaches detecting the ratio of binding of each probe to each target element, which permits the comparison of copy number (i.e. detection of aneuploidy) (column 2, lines

66-67 and column 3, lines 1-6) (claim 18). Therefore each and every element of these claims is met by the reference.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 18 and 26-28 rejected under 35 U.S.C. 103(a) as being unpatentable over Pinkel as applied to claims 18 and 26-27 above. Claims 18 and 26-27 are described above, and claim 28 further requires that said microparticles are silica microparticles.

Pinkel teaches all the limitations of claims 18 and 26-27. Also, while Pinkel does not explicitly state that the microparticles are silica microparticles, Pinkel does separately teach microparticles and covalently attaching the target nucleic acids to silica

(i.e. to form the binding agent). One of ordinary skill in the art would be motivated to use silica microparticles, because silica provides "a very low fluorescence substrate" and a "highly efficient hybridization environment" (column 9, lines 9-11), and the use of both microparticles and silica as the solid surfaces for the target nucleic acids provides a reasonable expectation that using silica microparticles would be successful. Therefore, it would have been prima facie obvious at the time the invention was made to use silica microparticles in a method of detecting aneuploidy, absent evidence to the contrary.

10. Claims 18-21, 23-24, 26-28 rejected under 35 U.S.C. 103(a) as being unpatentable over Pinkel as applied to claim 18 above, and further in view of Mohammed (Mohammed, US Patent Application Publication 2003/0124584). Claims 18 and 26-27 are described above. Claims 19-21 further require that said subject is a mammal selected from the group consisting of a human, a livestock animal, and an embryo. Claim 23 further requires that said embryo is generated using *in vitro* fertilization, and claim 24 further requires that said aneuploidy is detected in said embryo prior to implantation of said embryo.

Pinkel teaches all of the limitations of claim 18, as described above, however, Pinkel does not teach that the subject is a mammal selected from the group consisting of a human, a livestock animal, or an embryo; that said embryo is generated using *in vitro* fertilization; or that said aneuploidy is detected in said embryo prior to implantation of said embryo. Mohammed teaches a method of detecting aneuploidy, wherein said subject is mammal (page 2, paragraph 0015), said mammal is an embryo generated by

in vitro fertilization (page 13, paragraph 0119), and said method results in preimplantation genetic diagnosis (i.e. detection of aneuploidy prior to implantation of said embryo) (page 13, paragraph 0119). One of ordinary skill in the art would be motivated to use an embryo generated by *in vitro* fertilization as the subject prior to implantation of said embryo, as means to select against abnormal embryos prior to embryo transfer (page 113, paragraph 0119). Since preimplantation genetic diagnosis using embryos is already performed in the art and since the use of microparticles as one means of detecting aneuploidy is already taught by Pinkel, substituting a microparticle-based method as method of detecting aneuploidy has a reasonable expectation of success. Therefore it would have been prima facie obvious at the time the invention was made to use to use an embryo prior to implantation of said embryo as the subject in a method to detect aneuploidy, absent evidence to the contrary.

Mohammed also teaches a method of detecting genetic mosaicism (defined therein as "the presence of two or more chromosomally distinct cell lines" [page 13, paragraph 0118], i.e. detection of aneuploidy between cell lines) in livestock (page 13, paragraph 0120). One of ordinary skill in the art would be motivated to detect aneuploidy in livestock, because "screening founder animals for germline mosaicism prior to mating would reduce the costs associated with the propagation of transgenic lines" (page 13, paragraph 0120). Since testing for genetic mosaicism in livestock is already known in the art and since the use of microparticles as one means of detecting aneuploidy is already taught by Pinkel, substituting a microparticle-based method as a method of detecting aneuploidy/genetic mosaicism in livestock has a reasonable

expectation of success. Therefore, it would have been prima facie obvious at the time the invention was made to detect aneuploidy in livestock, absent evidence to the contrary.

11. Claims 18-22, 23-24, 26-28, and 34 rejected under 35 U.S.C. 103(a) as being unpatentable over Pinkel and Mohammed as applied to claims 18-21, 23-24, and 26-28 above, and further in view of Ibanez (Ibanez E, et al. Assessment of the proportion of transgene-bearing sperm by fluorescence in situ hybridization: a novel approach for the detection of germline mosaicism in transgenic male founders. Mol Reprod Dev. 2001 Feb;58(2):166-72). Claims 18-21, 23-24, and 26-28 are described above, and claims 22 and 34 further require that said subject is a livestock animal selected from the group consisting of cattle, sheep, and horses.

Pinkel and Mohammed teach a method of detecting genetic mosaicism (i.e. aneuploidy) in livestock, as described above. Pinkel and Mohammed do not teach that the livestock animal is selected from the group consisting of cattle, sheep, and horses. However, Ibanez teaches a method of detecting genetic mosaicism (pages 167-168) that can be used for cattle and sheep (page 166, see introduction; page 171, see conclusion). Again, one of ordinary skill in the art would be motivated to detect aneuploidy in livestock, and specifically cattle and sheep, because "screening founder animals for germline mosaicism prior to mating would reduce the costs associated with the propagation of transgenic lines" (Mohammed, page 13, paragraph 0120). Since testing for genetic mosaicism in livestock is already known in the art and described in Mohammed and since the use of microparticles as one means of detecting aneuploidy

is already taught by Pinkel, substituting a microparticle-based method as a method of detecting aneuploidy/genetic mosaicism in cattle or sheep has a reasonable expectation of success. Also, Ibanez suggests that a method of detecting genetic mosaicism used for mice would also work in cattle or sheep, further supporting that a method of detecting aneuploidy in cattle and sheep would be successful. Therefore it would have been prima facie obvious as the time the invention was made to detect aneuploidy in sheep or cattle, absent evidence to the contrary.

12. Claims 18-21, 23-28 rejected under 35 U.S.C. 103(a) as being unpatentable over Pinkel and Mohammed as applied to claims 18-21, 23-24, and 26-28, and in light of Gvakharia (Gvakharia M, et. al. Single in vitro fertilization (IVF) cycle with blastomere biopsy for preimplantation genetic diagnosis (PGD) of Huntington's disease, assisted hatching and cryopreservation results in healthy baby and subsequent ongoing pregnancy. Fertility and Sterility. 2002 Sept; 78(Supplement 1):S229). Claims 18-21, 23-24, and 26-28 are described above, and claim 25 further requires that said sample originate from a blastomere.

Pinkel and Mohammed teach all the limitations of claims 18-21, 23-24, and 26-28, as described above.

While Mohammed teaches that the sample be an embryo, Mohammed does not specifically state that the sample originated from a blastomere. However, Mohammed does state that the method is used for preimplantation genetic diagnosis, and it is standard technique in the art to collect cells from the blastomere stage to perform preimplantation genetic diagnosis. See, for example, Gvakharia. Therefore, one of

ordinary skill in the art would have been motivated to derive the sample from a blastomere and it would have been prima facie obvious at the time the invention was made to use cells from a blastomere in the method to detect aneuploidy as part of preimplantation genetic diagnosis. Since use of blastomeres is standard procedure for preimplantation genetic diagnosis, there is a reasonable expectation that use of blastomeres in any method for detecting aneuploidy would be successful, absent evidence to the contrary.

13. Claims 18, 26-29 rejected under 35 U.S.C. 103(a) as being unpatentable over Pinkel as applied to claims 18 and 26-28 above and in further view of Bitner (Bitner, et al. US Patent Number 6,787,307). Claims 18 and 26-28 are described above. Claim 28 further requires that said silica microparticles are silanized.

Pinkel teaches all the limitations of claims 18 and 26-28 as described above.

Pinkel does not teach that the silica microparticles are silanized. However, Bitner teaches a method of detecting nucleic acid sequences in a sample using silica microparticles that are silanized and coupled to nucleic acids. One of ordinary skill in the art would be motivated to use silanized silica microparticles in order to increase the binding of said polynucleotide to the microparticle. Also, because nucleic acid hybridization techniques and matrices have high fidelity under many circumstances, there is a reasonable expectation that the silanized silica microparticles used in the method of Bitner would be successfully used as the silica microparticles in the method of Pinkel. Therefore, it would have been prima facie obvious at the time the invention

was made for one of ordinary skill in the art to use silanized silica microparticles for the method of detecting aneuploidy of Pinkel, absent evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jaime M. Greene whose telephone number is 571-270-3052. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mary Mosher can be reached on 571-272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JMG 03/07/07

ZACHARIAH LUCAS
PATENT EXAMINER